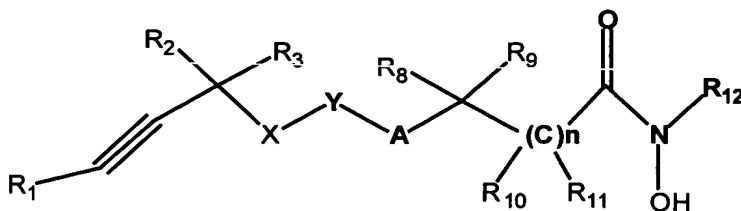


In the Claims

1. A compound of formula



wherein:

R₁ is hydrogen, aryl, heteroaryl, alkyl of 1-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or -C₄-C₈-cycloheteroalkyl;

R₂ and R₃ are each, independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH;

R₇ is hydrogen, aryl, aralkyl, heteroaryl, heteroaralkyl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -C(O)-R₁, -SO₂-R₁, -C(O)-NHR₁, -C(O)NR₅R₆, -C(O)R₁NR₅R₆, -C(O)-OR₁, -C(NH)-NH₂.

R₈, R₉, R₁₀, and R₁₁ are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs R₈ and R₉, R₉ and R₁₀ or R₁₀ and R₁₁, together with the carbon atom or atoms to which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C₄-C₈-cycloheteroalkyl ring;

R₁₂ is hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, or alkyl of 1-6 carbon atoms;

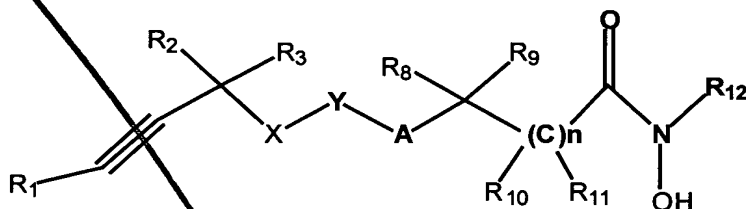
A is O, S, SO, SO₂, NR₇, or CH₂;

X is O, S, SO, SO₂, NR₇, or CH₂;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y;
and with the further proviso that if Y is phenyl, then R₈ and R₉ together with the
carbon atom to which they are attached may not form a piperdinyll or
tetrahydropyranyl ring; and

n is 0-2; or a pharmaceutically acceptable salt thereof.

4. A method of inhibiting pathological changes mediated by TNF- α converting enzyme
(TACE) in a mammal in need thereof which comprises administering to said mammal a
therapeutically effective amount of a compound having the formula



wherein:

R₁ is hydrogen, aryl, heteroaryl, alkyl of 1-8 carbon atoms, alkenyl of 2-6 carbon atoms,
alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or -C₄-C₈-
cycloheteroalkyl;

R₂ and R₃ are each, independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH₃;

R₇ is hydrogen, aryl, aralkyl, heteroaryl, heteroaralkyl, alkyl of 1-6 carbon atoms, alkenyl of
2-6 carbon atoms, alkynyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -
C(O)-R₁, -SO₂-R₁, -C(O)-NHR₁, -C(O)NR₅R₆, -C(O)R₁NR₅R₆, -C(O)-OR₁, -C(NH)-
NH₂.

R₈, R₉, R₁₀, and R₁₁ are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6
carbon atoms, -C₄-C₈-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18
carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs R₈
and R₉, R₉ and R₁₀ or R₁₀ and R₁₁, together with the carbon atom or atoms to
which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C₄-C₈-
cycloheteroalkyl ring;

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R_{12} is hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, or alkyl of 1-6 carbon atoms;

A3

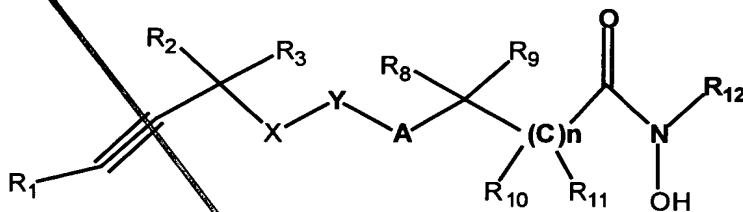
A is O, S, SO, SO₂, NR₇, or CH₂;

X is O, S, SO, SO₂, NR₇, or CH₂;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; and with the further proviso that if Y is phenyl, then R₈ and R₉ together with the carbon atom to which they are attached may not form a piperdinyl or tetrahydropyranyl ring; and

n is 0-2; or a pharmaceutically acceptable salt thereof.

6. A pharmaceutical composition comprising a compound having the formula



wherein:

R₁ is hydrogen, aryl, heteroaryl, alkyl of 1-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or -C₄-C₈-cycloheteroalkyl;

R₂ and R₃ are each, independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH₃;

R₇ is hydrogen, aryl, aralkyl, heteroaryl, heteroaralkyl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -C(O)-R₁, -SO₂-R₁, -C(O)-NHR₁, -C(O)NR₅R₆, -C(O)R₁NR₅R₆, -C(O)-OR₁, -C(NH)-NH₂.

*Sub-
gib-
AH*

~~R₈, R₉, R₁₀, and R₁₁ are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs R₈ and R₉, R₉ and R₁₀ or R₁₀ and R₁₁, together with the carbon atom or atoms to which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C₄-C₈-cycloheteroalkyl ring;~~

~~R₁₂ is hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, or alkyl of 1-6 carbon atoms;~~

~~A is O, S, SO, SO₂, NR₇, or CH₂;~~

~~X is O, S, SO, SO₂, NR₇, or CH₂;~~

~~Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; and with the further proviso that if Y is phenyl, then R₈ and R₉ together with the carbon atom to which they are attached may not form a piperdinyll or tetrahydropyranyll ring; and~~

~~n is 0-2; or a pharmaceutically acceptable salt thereof~~

Please cancel claim 3, without prejudice.

REMARKS

The present application is a divisional of 09/492,686. The specification has been amended to reflect the complete prosecution history. The claims have been amended to delete subject matter which has been allowed in the parent application.

Attached hereto is a marked-up version of the changes made to the application by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made."